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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/991,150 | 11/16/2001 | Avi J. Ashkenazi | P2730P1C48 | 4272 |

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EXAMINER

KEMMERER, ELIZABETH

ART UNIT PAPER NUMBER

1646

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 09/991,150 | ASHKENAZI ET AL. | |
| | Examiner | Art Unit | |
| | Elizabeth C. Kemmerer, Ph.D. | 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 124-126, 129-131 and 135-145 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 124-126, 129-131 and 135-145 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07 July 2004 has been entered. The Goddard and Ashkenazi declarations accompanying the response are also entered in full. Claims 1-123, 127, 128 and 132-134 are canceled. Claims 124-126, 129-131 and 135-145 are under examination

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 U.S.C. §§ 101 and 112, First Paragraph

Claims 124-126, 129-131 and 135-145 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 124-126, 129-131 and 135-145 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The bases for these rejections is of record (e.g., pp. 3-6 of the previous Office Action, mailed 21 January 2004).

Applicant's arguments (submitted with the amendment of 07 July 2004) have been fully considered but are not found to be persuasive for the following reasons.

Applicant reviews the evidentiary standard regarding the legal presumption of utility. Applicant argues that the USPTO has not met its burden of overcoming the presumption of the truth of an asserted utility. This has been fully considered but is not found to be persuasive. The examiner takes no issue with Applicant's discussion of the evidentiary standard regarding the legal presumption of utility. Furthermore, the rejection does not question the presumption of truth, or credibility, of the asserted utility. The asserted utilities of cancer diagnostics and cancer therapeutics for the claimed nucleic acids are credible and specific. However, they are not substantial. The data set forth in the specification are preliminary at best. As the courts have discussed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966), an asserted utility must exist in currently available form. The specification indicates that the PRO341 gene is amplified in only 3 out of 14 lung tumor samples. However, the literature reports that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy before the epithelial cells turn cancerous. See Hittelman (of record), who teach that damaged, precancerous lung epithelium is often aneuploid. See especially p. 4, Figure 4. The gene amplification assay in the specification does not provide a comparison between the lung tumor samples and normal lung epithelium, and thus it is not clear that PRO341 is amplified in

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cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium. One skilled in the art would not conclude that PRO341 is a diagnostic probe for lung cancer unless it is clear that PRO341 is amplified to a clearly greater extent in true lung tumor tissue relative to non-cancerous lung epithelium. Also, while it might be argued in hindsight that PRO341 would still be a marker at least for precancerous, or damaged, lung epithelium, such is not suggested by the specification as originally filed and is not well-established in the prior art.

Applicant urges that Hittelman supports utility of the claimed invention, asserting that the showing of DNA amplification of PRO341 DNA would be significant since it could lead to diagnosis of either a pre-cancerous state or squamous lung carcinoma itself. This has been fully considered but is not found to be persuasive. The specification as originally filed does not assert that the claimed nucleic acids can be used to diagnose a pre-cancerous state. The specification asserts that the claimed nucleic acids can be used as diagnostics or therapeutics for cancer. However, this asserted utility is not substantial, since significant further research would be required to establish a diagnostic nexus between the claimed nucleic acids and cancer.

Applicant argues the claims are now narrowly drawn to naturally occurring nucleic acids encoding PRO341 that are amplified in squamous cell carcinomas. Applicant urges that the specification details to the skilled artisan how to make and use nucleic acid variants for the diagnosis of squamous lung carcinoma. This has been fully considered but is not found to be persuasive. The claims are not limited to naturally occurring sequences. The claims are directed to any nucleic acid (natural or synthetic)

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encoding SEQ ID NO: 20 (e.g., claim 124), or small fragments (natural or synthetic) that hybridize to SEQ ID NO: 19 at defined conditions (e.g., claim 139). A large quantity of experimentation would be necessary to generate the infinite number of derivatives recited in the claims and possibly screen the same for activity. The specification does not provide direction/guidance regarding which structural features are required in order to provide activity. There are no working examples directed to variants. The nature of the invention (cancer diagnostics) is extremely complex. The state of the prior art establishes that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy before the epithelial cells turn cancerous, and thus extensive experimentation is required before a nexus between a nucleic acid (or its variants) and a cancer is established. Finally, the claims are quite broad, in that they fail to recite meaningful structural or functional limitations. upon consideration of all of these factors, it is determined that undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

For all of these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

This is a RCE of applicant's earlier Application No. 09/941,992. All claims are drawn to the same invention claimed in the earlier application and could have been

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finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D. can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ECK



ELIZABETH KEMMERER
PRIMARY EXAMINER